RESEARCH LETTER

Analysis of Neutralizing Antibody Levels in Children and Adolescents Up to 16 Months After SARS-CoV-2 Infection

Epidemiologic data indicate that SARS-CoV-2 infection in children is usually mild, which contrast with high rates of morbidity and mortality in older adults.1,2 Data on the strength and durability of antibodies generated after SARS-CoV-2 infection in children remain limited.3,4 Such data are critical in understanding disease severity, identifying risk of reinfection, and establishing herd immunity and vaccination policy. In this study, we analyzed the dynamics of neutralizing antibodies in a cohort of children and adolescents after SARS-CoV-2 infection. The study period covered the emergence of the original SARS-CoV-2 Wuhan strain up to including the Delta variant.

Methods | We recruited individuals aged 0 to 16 years with SARS-CoV-2 infection confirmed by polymerase chain reaction test with nasopharyngeal swabs at KK Women’s and Children’s Hospital in Singapore from February 1, 2020, to September 30, 2021. Participant follow-up included blood sampling or collection of residual blood sample from routine clinical care when available at various time points up to 16 months after infection. Ethical approval for this study was granted by Singhealth Centralised Institutional Review Board. Written informed consent was obtained for blood collection, and informed consent for public health research for collection of residual samples was waived. We followed the STROBE reporting guideline.

Serum of blood samples was tested with a surrogate viral neutralizing assay to detect neutralizing antibodies to SARS-CoV-2.5 We performed a biochemical measurement of the amount of neutralizing antibodies present in the test serum samples using inhibition enzyme-linked immunosorbent assay. We performed temporal distribution of neutralizing antibody levels since infection, with adjustment for age, sex, and symptom status.

Significance level was set at 2-sided \( P < .05 \). Data analysis was performed using R (R Core Team).

Results | Of the 126 study participants (mean [range] age, 7.4 years [1 month to 16 years]; 74 boys [58.7%], 52 girls [41.3%]), 38 (30%) completed 2 to 4 visits or blood sampling. All symptomatic cases (91 [72%]) were mild, with fever, cough, and runny nose as commonly reported symptoms. No cases were moderate or severe or developed into multisystem inflammatory syndrome in children.

Peak neutralizing antibody levels were reached at a median of 84% approximately 1 to 3 months after infection (Figure 1). Neutralizing antibody levels remained reasonably high with a median of 69.8% at 9 to 13 months after infection. In the adjusted analysis, neutralizing antibody levels by postinfection time were not associated with patient characteristics, such as sex and symptom status (Figure 2). However, during the acute phase of infection (<1 month), neutralizing antibody levels were highest in those younger than 5 years (71.6%; 95% CI, 58.5%-84.6%) and lowest in the 12 to 16 years group (49.9%; 95% CI, 41.3%-58.6%). Neutralizing antibodies in participants younger than 5 years remained little changed in the point estimates up to 16 months after infection.

Discussion | This study provided evidence of the durability of neutralizing antibodies in children up to 16 months after infection. There were no differences in level and duration of neutralizing antibodies by sex or symptom status. However, younger age (<5 years) was associated with significantly rapid generation of neutralizing antibody levels during the acute phase of infection and less degradation over time, compared with older age.

Study limitations included the assessment of neutralizing antibodies specific to viral spike protein receptor-binding domain as they were highly associated with protection.6 The sample size also decreased 9 months after infection, but all age groups were still represented.

The findings suggest that risk of SARS-CoV-2 reinfection in younger children is lower than in adults, which has important implications for scheduling COVID-19 vaccination...
after infection. The findings also broaden the understanding about less severe clinical disease in younger children.

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